DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
2098 Gaither Road
Rockville, MD 20850

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Via Federal Express

WARNING LETTER

Aurelio M. Fernandez
Chief Executive Officer
Institutional Review Board
Hialeah Hospital
651 East 25th Street
Hialeah, Florida 33013

Dear Mr. Fernandez:

The purpose of this Warning Letter is to inform you of objectionable conditions found during a Food and Drug Administration (FDA) inspection of your Institutional Review Board (IRB) and to request your prompt response. The inspection took place during the period of November 20 and 21, 2001, and was conducted by Mr. Victor Spanioli, an investigator from FDA's Florida District Office. The purpose of the inspection was to determine whether your procedures complied with Title 21, Code of Federal Regulations (21 CFR), Part 50-Protection of Human Subjects, Part 56-Institutional Review Boards, and Part 812 – Investigational Device Exemptions. These regulations apply to clinical studies of products regulated by the FDA.

Our review of the inspection report submitted by the district office revealed serious violations from pertinent regulations. Margaret R. Kane, Risk Manager and Infection Control Coordinator at Hialeah Hospital, received a Form FDA 483, "Inspectional Observations," at the conclusion of the inspection that listed the deviations noted and discussed with her. A copy of the Form FDA 483 is enclosed. The deviations noted include the following:

**Failure to maintain IRB membership as required by the regulations (21 CFR 56.107).**

When the IRB last met to review proposed investigational studies in 1998, there was no IRB member whose primary concern was non-scientific and all members were affiliated with Hialeah Hospital. Moreover, there was no IRB member familiar with applicable FDA regulations. Regulations require that an IRB have at least five (5) members with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. Specific requirements include at least one member whose primary concerns are in nonscientific areas; at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution; and membership competency as needed to ascertain the acceptability of specific research activities in terms of

institutional commitments and regulations, applicable law, and standards of professional conduct and practice.

**Failure to maintain adequate standard operating procedures (SOPs) governing the functions and operations of the IRB (21 CFR 56.108).**
At the time of the FDA inspection there were no written SOPs governing the functions and operations of the IRB. A copy of an incomplete draft of SOPs (copy enclosed) was supplied to the FDA investigator. Comments on that draft are enclosed.

**Failure to provide continuing review of approved studies (21 CFR 56.109(f)).**
Two studies that had been approved in 1998 received no continuing review by the IRB up to the time of the FDA inspection. An IRB is required to conduct continuing review of research at intervals appropriate to the degree of risk, but not less than once per year.

**Failure to maintain meeting minutes in sufficient detail (21 CFR 56.115(a)(2)).**
There was no documentation in meeting minutes that the two studies approved in 1998 had received the required in-depth review and discussion by the IRB prior to their approval. Meeting minutes also fail to include specifics regarding voting on proposed research in that they do not contain the numbers of members voting for, against, and abstaining.

**Failure to maintain the proper information about IRB members (21 CFR 56.115(a)(5)).**
The required information was not available at the time of the FDA inspection. Required information includes a list of members identified by name; earned degrees; representative capacity; indications of experience, such as board certifications, licenses, etc. sufficient to describe each member's chief anticipated contributions to IRB deliberations; and any employment or other relationship between each member and the institution.

The deviations listed above are not intended to be an all-inclusive list of the deficiencies noted. The IRB is responsible for adhering to each requirement of the law and relevant regulations.

The inspection report notes that the IRB is currently essentially inactive. No new studies have been approved since 1998. A recently approved study, for the use of Innohep®, which is taking place at Hialeah Hospital was reviewed by Western Institutional Review Board (WIRB) instead. Additionally, Ms. Kane is quoted as stating that the hospital intends to correct all IRB deficiencies within six months and will not review or approve any studies until compliance is achieved.

Within fifteen (15) working days of receipt of this letter, please inform FDA of the status of the corrective actions taken to remedy the deficiencies noted. Please provide for FDA review your finalized SOPs; a listing of current IRB members that includes individual information required by the regulations; a listing of alternate members and their required information, if the IRB chooses to use alternates; and examples of all forms and boilerplates the IRB plans to use for communicating with clinical investigators. If some or all of this information is not currently available, please include a timeframe in which we can expect to receive them.

Please send the information requested to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, Program Enforcement Branch II (HFZ-312), 2098 Gaither Road, Rockville, Maryland 20850, Attention: Jean Toth-Allen, Ph.D. Failure to respond can lead to further regulatory actions, including, as described in 21 CFR 56.120 and 56.121, withholding approval of new studies, directing that no new subjects be added to on-going studies, terminating on-going studies, notifying relevant State and Federal regulatory agencies, and disqualification of the IRB.

A copy of this letter has been sent to FDA's Florida District Office, 555 Winderley Place, Suite 200, Maitland, Florida 32751. We request that a copy of your response also be sent to that office.

If you have any questions, feel free to contact Jean Toth-Allen at (301) 594-4723, extension 141.

Sincerely yours,

Larry Spears
Acting Director
Office of Compliance
Center for Devices and Radiological Health

Enclosures